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## INVITED REVIEW

Male Fertility

# Recurrent varicocele

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**Varicocele recurrence is one of the most common complications associated with varicocele repair. A systematic review was performed to evaluate varicocele recurrence rates, anatomic causes of recurrence, and methods of management of recurrent varicoceles. The PubMed database was evaluated using keywords “recurrent” and “varicocele” as well as MESH criteria “recurrent” and “varicocele.” Articles were not included that were not in English, represented single case reports, focused solely on subclinical varicocele, or focused solely on a pediatric population (age <18). Rates of recurrence vary with the technique of varicocele repair from 0% to 35%. Anatomy of recurrence can be defined by venography. Management of varicocele recurrence can be surgical or via embolization.**

*Asian Journal of Andrology* (2016) 18, 229–233; doi: 10.4103/1008-682X.171578; published online: 15 January 2016

**Keywords:** infertility; recurrence; varicocele

## INTRODUCTION

Varicoceles are defined as dilation of the veins of the pampiniform plexus. They are found in approximately 15% of adolescent male subjects and in >30% of men evaluated for infertility.<sup>1,2</sup> They represent a reversible cause of male factor infertility. Diagnosis of clinical varicocele is made by physical examination. Indications for varicocele surgery include testicular hypotrophy, infertility, and scrotal pain. Methods for correction of varicoceles are open surgical, laparoscopic, or percutaneous techniques.

One of the most common complications with varicocele surgery is varicocele recurrence. Recurrence rates vary widely and may be dependent on the population being studied (e.g., pubertal vs adult), indications for initial intervention (e.g., testicular atrophy vs infertility vs pain), degree of initial varicocele (e.g., subclinical vs clinical), technique employed (e.g., open vs laparoscopic vs percutaneous), definition of recurrence (e.g., clinical vs subclinical), and follow-up period. To determine rates of varicocele recurrence following various treatment methods among infertile men as well as to evaluate methods of treatment of recurrence in this population, a systematic literature review was performed.

## METHODS

A literature search was performed in the PubMed database using MESH criteria “varicocele” and “recurrence” as well as terms “varicocele” and “recurrence.” Most PubMed data are from 1966 on but the database includes selected records dating back earlier. No date constraints were placed on the PubMed query, which was performed during August 2015. All published articles were evaluated and exclusion criteria for search included nonhuman subjects and non-English articles. Using PubMed terms, 254 articles were identified and using MESH criteria, 125 articles were identified with many overlapping articles. Articles were then evaluated and excluded if they represented single case reports, focused solely on subclinical varicoceles, focused on nontesticular varicoceles, failed to mention recurrence rates or focused solely on pediatric

population. Data on recurrence rates, type of varicocele repair, anatomic cause of recurrence, and management of recurrence were recorded. We also searched the references of included studies to identify additional, potentially relevant studies. Included articles were grouped by method of repair evaluated and whether focus was on initial or recurrent varicocele population. Data were extracted from included articles as it related to recurrence rates after various techniques, anatomy/causes of recurrent varicocele, and treatment outcomes after recurrent varicocele repair. **Table 1** provides a list of the studies evaluated.

## RATES OF RECURRENT VARICOCELE

A systematic review performed from 1980 to 2008 identified 36 studies reporting outcomes of varicocele treatment in infertile men with palpable unilateral or bilateral varicocele and abnormal semen parameters without azoospermia.<sup>3</sup> Of these, 16 studies looked at recurrence rate as an outcome. Various surgical techniques were employed, and published rates of recurrence for each were compared. Four studies employed the retroperitoneal high ligation (Palomo) technique and overall recurrence rate for this method was cited at 14.97% (7%–35%).<sup>4–7</sup> Ten studies employed a microsurgical approach (6 sub-inguinal and 4 inguinal) finding an overall recurrence rate of 1.05% (0%–3.57%).<sup>5,6,8–13</sup> Two studies employed a macroscopic inguinal or sub-inguinal approach citing an overall recurrence rate of 2.63% (0%–37%).<sup>7,14</sup> Five studies evaluated the laparoscopic approach and found an overall recurrence rate of 4.3% (2.17%–7.14%).<sup>5,15–18</sup> Finally, two studies looked at radiologic embolization for varicocele and found an overall recurrence rate of 12.7% (2%–24%).<sup>7,19</sup> The mean follow-up, for those studies that listed it, ranged from 6 to 25 months. The authors concluded that open microsurgical inguinal or sub-inguinal varicocelectomy led to the fewest recurrences, which they attributed to the ability of the surgeons to visualize and ligate all spermatic veins with the higher magnification.<sup>3</sup>

Another recent meta-analysis identified randomized controlled trials comparing open nonmicrosurgical, laparoscopic, or microsurgical

**Table 1: List of studies included in the review of recurrent varicocele**

<i>Authors</i>	<i>Title</i>	<i>Year published</i>	<i>Study design</i>	<i>Sample size</i>
Cayan <i>et al.</i>	Comparison of results and complications of high ligation surgery and microsurgical high inguinal varicocelectomy in the treatment of varicocele	2000	Randomized control trial	468
Watanabe <i>et al.</i>	Minimal invasiveness and effectivity of sub-inguinal microscopic varicocelectomy: a comparative study with retroperitoneal high and laparoscopic approaches	2005	Retrospective review	144
Ghanem <i>et al.</i>	Sub-inguinal microvaricocelectomy versus retroperitoneal varicocelectomy: comparative study of complications and surgical outcome	2004	Retrospective review	413
Yavetz <i>et al.</i>	Efficacy of varicocele embolization versus ligation of the left internal spermatic vein for improvement of sperm quality	1992	Randomized control trial	137
Jungwirth <i>et al.</i>	Clinical outcome of microsurgical sub-inguinal varicocelectomy in infertile men	2001	Retrospective review	272
Orhan <i>et al.</i>	Comparison of two different microsurgical methods in the treatment of varicocele	2005	Retrospective review	212
Kumar and Gupta	Sub-inguinal microsurgical varicocelectomy: evaluation of the results	2003	Retrospective review	90
Marmar and Kim	Sub-inguinal microsurgical varicocelectomy: a technical critique and statistical analysis of semen and pregnancy data	1994	Retrospective review	466
Ito <i>et al.</i>	Results obtained from microsurgical therapy of varicocele	1993	Retrospective review	56
Goldstein <i>et al.</i>	Microsurgical inguinal varicocelectomy with delivery of the testis: an artery and lymphatic sparing technique	1992	Retrospective review	465
Ross and Ruppman	Varicocele vein ligation in 565 patients under local anesthesia: a long-term review of technique, results and complications in light of proposed management by laparoscopy	1993	Retrospective review	565
Mehan <i>et al.</i>	Laparoscopic internal spermatic vein ligation: report of a new technique	1992	Retrospective review	51
Enquist <i>et al.</i>	Laparoscopic versus sub-inguinal varicocelectomy: a comparative study	1994	Retrospective review	47
Jarow <i>et al.</i>	Effectiveness of laparoscopic varicocelectomy	1993	Retrospective review	46
Milad <i>et al.</i>	Laparoscopic varicocelectomy for infertility. An initial report from Saudi Arabia	1996	Retrospective review	48
Nabi <i>et al.</i>	Percutaneous embolization of varicoceles: outcomes and correlation of semen improvement with pregnancy	2004	Retrospective review	102
Al-Kandari <i>et al.</i>	Comparison of outcomes of different varicocelectomy techniques: open inguinal, laparoscopic, and sub-inguinal microscopic varicocelectomy: a randomized clinical trial	2007	Randomized control trial	120
Al-Said <i>et al.</i>	Varicocelectomy for male infertility: a comparative study of open, laparoscopic, and microsurgical approaches	2008	Randomized control trial	298
Abdel-Maguid and Othman	Microsurgical and nonmagnified sub-inguinal varicocelectomy for infertile men: a comparative study	2010	Randomized control trial	162
Ding <i>et al.</i>	Open nonmicrosurgical, laparoscopic or open microsurgical varicocelectomy for male infertility: a meta-analysis of randomized controlled trials	2012	Systematic review	1015
Chung <i>et al.</i>	Minilaparoscopic varicocelectomy with preservation of testicular artery and lymphatic vessels by using intracorporeal knot-tying technique: 5-year experience	2011	Retrospective review	87
Shiraishi <i>et al.</i>	Comparison of the results and complications of retroperitoneal, microsurgical sub-inguinal, and high inguinal approaches in the treatment of varicoceles	2012	Retrospective review	353
Kim <i>et al.</i>	Outcomes of microsurgical sub-inguinal varicocelectomy for painful varicoceles	2012	Retrospective review	81
Gandini <i>et al.</i>	Male varicocele: transcatheter foam sclerotherapy with sodium tetradecyl sulfate – outcome in 244 patients	2008	Retrospective review	244
Li <i>et al.</i>	Safety and effectiveness of transcatheter foam sclerotherapy for testicular varicocele with a fluoroscopic tracing technique	2010	Retrospective review	58
Galfano <i>et al.</i>	Surgical outcomes after modified antegrade scrotal sclerotherapy: a prospective analysis of 700 consecutive patients with idiopathic varicocele	2008	Retrospective review	697
Misseri <i>et al.</i>	The adolescent varicocele II: the incidence of hydrocele and delayed recurrent varicocele after varicocelectomy in a long-term follow-up	2001	Retrospective review	77
Lund <i>et al.</i>	Clinical assessment after varicocelectomy	2000	Retrospective review	15
Franco <i>et al.</i>	Challenging the role of cremasteric reflux in the pathogenesis of varicocele using a new venographic approach	1999	Retrospective review	73
Moon <i>et al.</i>	Recurrent varicoceles: causes and treatment using angiography and magnification assisted sub-inguinal varicocelectomy	2012	Retrospective review	15
Sze <i>et al.</i>	Persistent and recurrent postsurgical varicoceles: venographic anatomy and treatment with N-butyl cyanoacrylate embolization	2008	Retrospective review	17
Jargiello <i>et al.</i>	Endovascular transcatheter embolization of recurrent postsurgical varicocele: anatomic reasons for surgical failure	2015	Retrospective review	33
Gorur <i>et al.</i>	Low body mass index may be a predisposing factor for varicocele recurrence: a prospective study	2015	Retrospective review	255
Grober <i>et al.</i>	Microsurgical treatment of persistent or recurrent varicocele	2004	Retrospective review	54
Madjar <i>et al.</i>	Low inguinal approach for correction of recurrent varicocele	1998	Retrospective review	23
Chawla <i>et al.</i>	Microsurgical varicocelectomy for recurrent or persistent varicoceles associated with orchalgia	2005	Retrospective review	12
Mazzoni <i>et al.</i>	Recurrent varicocele: role of antegrade sclerotherapy as first choice treatment	2002	Retrospective review	53
Kim <i>et al.</i>	Persistent or recurrent varicocele after failed varicocelectomy: outcome in patients treated using percutaneous transcatheter embolization	2012	Retrospective review	28
Feneley <i>et al.</i>	Retrograde embolization and causes of failure in the primary treatment of varicocele	1997	Retrospective review	154
Chen	Predictive factors of successful redo varicocelectomy in infertile patients with recurrent varicocele	2014	Retrospective review	48



varicoectomy procedures in adults with male infertility. The included patients had to have been infertile >12 months with a clinically palpable varicocele, a defect in semen analysis and where the female partner had a normal examination. Only four studies were found to meet inclusion criteria, and a total of 1015 patients were evaluated.<sup>4,20–23</sup> Mean follow-up for these studies was 18 months (11–26), 21 months (4–35) and 17.4 months. The final study did not list a mean follow-up period but stated that patients were evaluated at 4 and 12 months. The pooled data revealed the incidence of recurrent varicocele to be 17.2% (34/198 cases) for laparoscopic technique, 1.9% (10/518 cases) for microscopic technique, and 13.7% (68/497 cases) for open technique. This was significantly lower after microsurgery than after laparoscopic or open varicoectomy (OR = 0.12, 95%CI 0.06, 0.32 and OR = 0.13, 95%CI 0.07, 0.25, respectively), while there was no significant difference between laparoscopic and open varicoectomy (OR = 1.55, 95%CI 0.88, 2.76). The authors again concluded that the microsurgical technique led to a significant reduction in postoperative recurrence, which they attributed to the fact that all internal and external spermatic veins can be ligated. Of note, due to a lack of studies, the differences between surgical approaches and embolization were not evaluated.<sup>23</sup>

More recent studies have shown rates of recurrence that are within range of those reported in the prior meta-analysis for laparoscopic (1.2%), nonmagnified inguinal (1.3%), open retroperitoneal (9.3%), microsurgical sub-inguinal (0.9%–2.5%), retrograde sclerotherapy (3.6%–8.6%), and antegrade sclerotherapy (9%) approaches with variable study criteria.<sup>24–29</sup>

It is important to note that the length of follow-up time could significantly affect the recurrence rate. A study in the pediatric population found new recurrences after open repairs 15, 37, and 76 months out that were not palpated at 3, 14, and 63 months respectively.<sup>30</sup>

The clinical skills of the examining clinician may also affect the diagnosis of recurrent varicocele. A study of 15 patients whom had previously undergone laparoscopic varicoectomy for grade III varicocele with asymmetry sought to determine clinical recurrence rate by four physicians with different levels of training. The patients also had a color Doppler ultrasound performed by a single operator. The four examiners determinations of recurrence had a positive predictive value ranging from 0.56 to 0.71, negative predictive value ranging from 0.67 to 1.00, sensitivity ranging from 0.71 to 1.0 and specificity ranging from 0.5 to 0.75. Therefore, the authors concluded that there was significant variability between clinical assessment and ultrasound results and recommended that ultrasound be used in every case of varicocele to give the most accurate diagnosis. However, the recurrence rate by ultrasound examination, which was considered the gold standard, was 80% (12/15) at a follow-up of 6–48 months. This is much higher than other published rates. In addition, the variability among observers was not listed and the difference seen between examination and ultrasound likely represents subclinical disease.<sup>31</sup> This suggests that ultrasound should not be routinely relied on for the diagnosis of recurrent varicocele.

### CAUSES OF RECURRENT VARICOCELE

The reason for varicocele recurrence is often attributed to the surgical technique employed. As in the above studies, the higher rates of failure seen with macroscopic inguinal or sub-inguinal varicoectomy are theorized to be secondary to missed smaller internal spermatic veins that later dilate and cause recurrence. The higher recurrence rate seen with the open retroperitoneal or laparoscopic approaches is often attributed to the inability to ligate external gonadal (cremasteric) vessels

or the external spermatic vein in these procedures. Early studies by Coolsaet suggested that up to one-third of all patients with varicocele had reflux into the extrafunicular veins (cremasteric, external pudendal, deferential)<sup>32</sup> but the belief that varicocele or varicocele recurrence can be due to reflux into extrafunicular veins has been widely debated.

A 1999 study sought to demonstrate the presence of reflux in extrafunicular veins in patients with recurrent varicocele. Of 73 patients studied, 19 presented with recurrence after previous surgical correction (high ligation, inguinal ligation, or microsurgical spermatic epigastric vein shunt). All underwent left iliac vein venography, and a patent internal spermatic vein was demonstrated in all 19 recurrent cases. The authors concluded that “recurrent varicocele is due to persisting or recurrent reflux in the internal spermatic vein and that concomitant dilatation of the extrafunicular veins does not justify ligation.”<sup>33</sup>

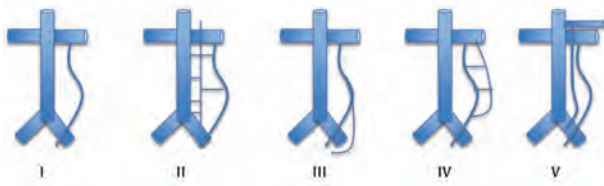
A recent study identified 15 patients with recurrent varicocele. The population was heterogeneous with varied ages (12–42), varied initial treatments and initial indications. Recurrence was determined by physical examination and ultrasound. 11 of the 15 underwent preoperative angiography (3 refused, 1 had contrast allergy). Of those 11, 7 were found to have patent internal spermatic veins and underwent embolization. 39% without patent veins on angiography ( $n = 4$ ) underwent loupe-assisted or microsurgical sub-inguinal repair. In these cases, dilated internal spermatic veins in combination with dilated external spermatic or gubernacular veins were seen despite no evidence on angiography.<sup>34</sup> It is unclear if the dilated external spermatic or gubernacular veins were causing recurrence or just dilated from increased flow of venous blood following ligation of the internal spermatic veins during the initial varicocele surgery.

A study of 17 patients undergoing endovascular embolization for recurrent postsurgical varicocele retrospectively sought to evaluate the venous anatomy in even greater detail. The authors used the anatomic categorization previously described in works by Bühren *et al.* and Sigmund *et al.*<sup>35,36</sup> (Table 2 and Figure 1). The patients varied in age (13–54 years), indication, length of time since varicoectomy (mean 48 months) and previous treatment method utilized. Eleven of seventeen patients evaluated exhibited Bühren type III anatomy with collaterals draining into a single gonadal vein with duplications being found most frequently in the pelvis and inguinal canal. Two patients each exhibited type I and type II anatomy and 1 patient each exhibited type IV and type V anatomy. Sixteen of seventeen patients had successful embolization without recurrence. The authors concluded that redundancies of the gonadal veins near the inguinal canal appear to be responsible for the majority of postsurgical recurrent varicoceles.<sup>37</sup>

A very similar study was performed on 33 men with recurrent varicocele after surgical intervention. They underwent venography

**Table 2: Bühren *et al.*<sup>35</sup> classification of types of varicocele, published in 1983**

Classification	Description
0	No reflux in gonadal vein
I	Reflux in single incompetent gonadal vein
II	Reflux to the main single gonadal vein tributary via multiple collaterals to lumbar or iliac veins, perivertebral venous plexus, or to inferior vena cava
III	Reflux to a duplicated gonadal vein where duplication can occur in the superior, inferior or middle portion of the vein
IV	Reflux through renal hilar or capsular veins when the renal-gonadal vein junction valve is competent
V	Reflux into a gonadal vein drained by an additional (doubled) renal vein



**Figure 1:** Schematic of Bühren *et al.*<sup>35</sup> classification of types of varicocele, published in 1983.

before embolization and it was again found that the majority of patients (66%) had a type III duplication and that no recurrences were seen after embolization in a mean 14-month follow-up. Interestingly, the study did find that the redundancies of the gonadal vein tended to occur in the mid-portion of the vein (39%) in contrast from the previous study where the majority were seen low near the inguinal canal.<sup>38</sup>

Although technique is often cited as the most likely contributing factor to recurrence, one study of 255 men evaluated with primary infertility found that lower body mass index might be an independent predisposing factor for varicocele recurrence. The BMI score of the recurrent varicocele group ( $24.8 \pm 2.9$ ) in this study of infertile men with clinical varicoceles who underwent open sub-inguinal varicocelectomy, was significantly lower than that of the nonrecurrent or control group ( $26.9 \pm 2.9$ ) ( $P < 0.001$ ). They determined that a one-unit decrease in BMI score correlated with a 1.25 times increased risk of varicocele recurrence using a logistic regression model. The authors concluded that low BMI could be an indicator for performing a microsurgical technique to lower risk of recurrence.<sup>39</sup>

### TREATMENT OF RECURRENT VARICOCELE

Few studies address effectiveness of different approaches in treating recurrent varicoceles when they occur and to our knowledge no head-to-head or randomized controlled trials exist. The studies evaluating the treatment of recurrent varicoceles are invariably small, uncontrolled and include a heterogeneous population.

Three studies were identified that looked at surgical treatment and two studies reported embolization of recurrent varicoceles. One looked at 54 men referred for recurrent varicocele who underwent testicular artery and lymphatic-sparing sub-inguinal microsurgical varicocelectomy for varicocele recurrence. The initial treatment method varied with 74% having had nonmicrosurgical inguinal varicocelectomy, 10% having had retroperitoneal high ligation, 4% having undergone microsurgical inguinal varicocelectomy, and 2% having undergone nonmicrosurgical sub-inguinal varicocelectomy. Age (16–52 years) and initial indication also varied in this population. Mean serum testosterone, mean testicular volume, median sperm concentration, percent motility, and total motile sperm per ejaculate all improved significantly after repeat varicocelectomy. No recurrences were seen and an overall pregnancy rate of 40% was achieved (via natural insemination, IUI and IVF) in a mean 24 weeks follow-up.<sup>40</sup> Another identified 23 patients with clinical recurrences after high retroperitoneal or transinguinal ligation who underwent subsequent open varicocelectomy with a macroscopic sub-inguinal approach. Recurrence after redo operation was diagnosed based on both clinical examination and scrotal radioisotope scan and 21/23 (91.3%) men had no recurrence with 1-year follow-up. 19/23 (82.6%) had marked improvement in semen parameters while two more had a minor improvement.<sup>41</sup> The third publication reported on 12 patients with recurrent clinical varicoceles after “nonmicrosurgical varicocelectomy”

specifically associated with orchalgia. The method used for prior varicocelectomy was not reported. All underwent microsurgical sub-inguinal varicocelectomy and no recurrences were seen at a mean 12 months follow-up. An overall favorable pain response was seen in 10/11 patients with 6 reporting complete resolution. No mention of semen parameters was made.<sup>42</sup>

Two studies were identified that looked at outcomes of recurrent varicocele treated with embolization. The first looked at 53 patients with recurrent varicocele who underwent antegrade sclerotherapy. The population was mixed in terms of age, indication and previous varicocele treatment method. Overall 2 out of 49 (4.1%) patients who were followed for a minimum of 6 months were found to have recurrence. Fertility parameters were not assessed.<sup>43</sup> A second evaluated 28 patients who had recurrent varicocele after laparoscopic, retroperitoneal, or inguinal ligation. Embolization was technically feasible in all but two cases (93%) and one patient was lost to follow-up. In the remaining 25 cases, 80% had complete resolution on physical examination, 16% had partial improvement, and 4% had no improvement at a median follow-up of 195 days. Semen parameters were not assessed.<sup>44</sup>

Two studies of patients undergoing antegrade sclerotherapy and retrograde embolization for varicocele also included a small subpopulation of patients who were being treated for recurrent varicocele. In those subanalyses, success rates of 92.5% and 77.8%, respectively were seen.<sup>29,45</sup>

An additional study of 48 infertile men with recurrent varicoceles attempted to retrospectively determine risk factors for unsuccessful repeat varicocelectomy. The patients were grouped into those who had improvement in semen parameters after repeat microsurgical sub-inguinal varicocelectomy ( $n = 21$ ), those who did not have improvement after repeat microsurgical sub-inguinal varicocelectomy ( $n = 17$ ), and those who chose not to undergo repeat varicocelectomy ( $n = 10$ ). They reported that the significant predictive factors associated with successful redo varicocelectomy were lower follicle-stimulating hormone levels, lower peak retrograde flow on Doppler ultrasound, longer time to recurrence of varicocele, larger testicular volume preoperatively, and higher number of ligated veins during redo varicocelectomy.<sup>46</sup>

Without randomized studies and with the variable nature of each study drawing conclusions is difficult at best. Based on the data available, identifying an ideal method for treatment of recurrent varicocele is not possible.

### EXPERT COMMENTARY

Based on the above reports, it is clear that the major reason for varicocele recurrence is the persistence of branched spermatic veins that were not ligated during the initial repair. While recurrence due to cremasteric, vasal, or gubernacular veins may be possible, current studies do not support a role for these veins in recurrence in the majority of patients. Many of the branches involved in recurrent varicoceles branch above the sub-inguinal level that may be why sub-inguinal approaches generally have the lowest varicocele recurrence rates.

At our institution, the initial treatment for infertile men with abnormal semen analysis and clinical varicocele is the microsurgical sub-inguinal approach without testicular delivery. This choice is based on the current evidence, which strongly suggests the lowest recurrence rates with this approach. Most of the studies employing surgical treatment of recurrent varicoceles used retroperitoneal or inguinal approaches for the initial approach. In those cases, a sub-inguinal approach would be technically feasible. However, if the initial approach



were a sub-inguinal technique, repeat sub-inguinal surgery would be difficult and risk injuring the arterial supply of the testis. Because of this, we usually utilize embolization in these cases.

### KEY ISSUES

- Current evidence suggests that the initial treatment method most likely to prevent recurrences in an infertile man with a clinical varicocele is the microsurgical sub-inguinal or inguinal varicocelectomy
- Varicocele recurrence is most commonly due to branches of the internal spermatic veins that were not initially ligated
- Treatment of recurrence is warranted only in those patients with clinical recurrence that remain infertile or symptomatic
- No strong evidence exists to suggest the ideal treatment for the recurrent varicocele and further randomized studies would be necessary to answer this question.

### AUTHOR CONTRIBUTIONS

KR and MS worked to research the topic and draft the manuscript. All authors have read and approved the final version of the manuscript.

### COMPETING INTERESTS

None of the authors declare competing financial interests.

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